

Serial No.: 08/333,690
Docket No.: 7639-061 (Cell 16.0)

FILED: November 3, 1994

APPENDIX A -- PENDING CLAIMS

37. A replication-defective recombinant adenovirus, wherein the genome of said adenovirus contains at least two lethal deletions, two lethal mutations, or one lethal deletion and one lethal mutation in the E1 and E4 early gene regions, so that the recombinant adenovirus requires for replication complementation of genes of both the E1 and E4 adenoviral early regions, wherein said recombinant adenovirus genome additionally contains a transgene.

38. A replication-defective recombinant adenovirus, wherein the genome of said adenovirus contains at least two lethal deletions, two lethal mutations, or one lethal deletion and one lethal mutation in the E1 and E4 early gene regions, wherein an essential region of the E4 early gene region is deleted or mutated, so that the recombinant adenovirus requires for replication complementation of genes of both the E1 and E4 adenoviral early regions, and wherein said recombinant adenovirus genome additionally contains a transgene.

39. A packaging cell line derived from a 293 cell that supports the growth of a replication defective recombinant adenovirus that carries at least a lethal deletion in each of adenovirus E1 and E4 early gene regions, so that the recombinant adenovirus requires for replication

— *Exhibit A* —

complementation of genes of both the E1 and E4 adenoviral early regions, comprising a cell line that supplies the function of the E1 early region and the E4 early region wherein nucleotide sequences encoding the E1 and E4 early regions are operably linked to an inducible promoter.

40. A DNA plasmid comprising an inducible promoter operably linked to nucleotide sequences encoding a cytotoxic gene product of an adenoviral E4 gene or E4 early gene region.

41. The DNA plasmid of Claim 40 wherein said inducible promoter is a promoter from a cAMP response element binding protein regulated gene.

42. The DNA plasmid of Claim 41 wherein said inducible promoter is selected from a gene encoding mammalian alpha inhibin.

43. The DNA plasmid of Claim 41 wherein said inducible promoter is selected from a gene encoding mouse alpha inhibin.

44. The DNA plasmid of Claim 40 wherein said inducible promoter is selected from a gene encoding a tetracycline responsive promoter.

45. The plasmid pIK6.1 MIP(α)-E4 designated ATCC #75879.

46. A recombinant adenoviral vector, wherein said vector comprises at least a lethal deletion or mutation in two gene

regions selected from the group consisting of E1, E2A, E4 early gene regions, viral structural genes, and additionally comprises a transgene so that when rescued the resulting recombinant adenovirus requires for replication complementation of genes of both the E1 and E4 adenoviral early regions.

47. A recombinant adenoviral vector comprising at least a lethal deletion in each of adenovirus E1 and E4 early gene regions, and a transgene so that when rescued the resulting recombinant adenovirus requires for replication complementation of genes of both the E1 and E4 early regions.

48. A packaging cell line derived from a 293-cell that supplies the function of the E2A and E4 early region wherein the nucleotide sequences encoding the E2A or the E4 early region are operably linked to an inducible promoter and that supports the growth of a mutant adenovirus defective in replication, wherein said adenovirus comprises at least a lethal deletion or mutation in two gene regions selected from the group consisting of E1, E2A, E4 early gene regions, viral structural genes, and so that when rescued the resulting recombinant adenovirus requires for replication complementation of genes of both the E1 and E4 early regions.

49. A packaging cell line derived from a 293 cell that supplies the function of the E2A and E4 early region wherein the nucleotide sequences encoding the E2A or the E4 early region are operably linked to an inducible promoter and that

supports the growth of a recombinant adenoviral vector comprising a transgene, wherein said vector comprises at least a lethal deletion or mutation in two gene regions [two lethal deletions, two lethal mutations or one lethal deletion and one lethal mutation] selected from the group consisting of E1, E2A, E4 early gene regions, viral structural genes, so that when rescued the resulting recombinant adenovirus requires for replication complementation of genes of both the E1 and E4 early regions.

50. A packaging cell line derived from a 293 cell that supplies the function of the E4 early region wherein the nucleotide sequences encoding the E4 early region are operably linked to an inducible promoter and that supports the growth of an adenoviral vector, wherein said vector comprises a lethal deletion or mutation in each of the E1 and E4 early gene regions of said adenoviral vector and a transgene so that when rescued the resulting recombinant adenovirus requires for replication complementation of genes of both the E1 and E4 early regions.

52. The replication-defective recombinant adenovirus of Claim 38 in which the region of the E4 early gene region which is deleted or mutated is open reading frame 6.

54. The recombinant adenovirus of Claim 46 in which the region of the E4 early gene region which is deleted or mutated is open reading frame 6.

Claim 55 canceled.

56. The recombinant adenoviral vector of Claim 46 or 47 which further comprises a deletion of the E3 gene region.

57. The packaging cell line of Claim 48, 49, or 50 which supports the growth of the recombinant adenoviral vector which further comprises a deletion of the E3 gene region.